Ex. A

EIGHTEENTH EDITION

Zinsser Microbiology

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Epidemiology

In susceptible populations, mumps virus infection is predominantly a disease of childhood, with the majority of clinically evident infections being seen between the ages of 5 and 10 years. It has been estimated that in the prevaccine era 90 percent of the population were immune by the time they reached 15 years of age. Although mumps virus infection is contagious, it is less communicable than measles and varicella. The degree of communicability is estimated most accurately by serologic surveys of exposed individuals because as many as one fourth of the infections with mumps virus occur without clinical symptoms.

Isolation of the patient within the hospital setting or in homes, when it is attempted, has not effectively curtailed spread of disease. This is usually attributed to the period of virus shedding that occurs prior to the symptomatic onset of illness and thus precedes the recognition of infection. As previously mentioned, one fourth of patients have an asymptomatic infection, but they also excrete virus. Their infection is self-limited, and their immunity is comparable to those with symptomatic infection. To the best of our knowledge, there are no animal reservoirs or human carriers of mumps virus.

Diagnostic Approach

The work of Johnson and Goodpasture first established that mumps was caused by a filterable virus and demonstrated that rhesus monkeys could be experimentally infected. The description of the complement-fixation test and successful propagation of virus in chick embryo preceded the now generally employed standard tissue culture techniques. These methods employ monolayers of one of several cell types, including primary monkey kidney, human amnion, or human kidney and cell lines, such as HeLa. In vitro multinucleate giant cells are seen, and hemabsorption inhibition provides a practical means of identification of the virus. With these techniques, virus has been isolated from such varied sources as blood, cerebrospinal fluid, urine, saliva, salivary gland tissue, and human milk.

In many academic and large hospital settings, viral diagnostic laboratories are available, and virus isolation can be attempted from clinical materials. The responsible laboratory will provide directions for submitting materials for culture. Saliva and urine can be collected at the time of clinical central nervous system symptoms and submitted for culture. Mumps isolation in tissue culture is usually not necessary for either diagnosis or management of patients with parotitis, but the techniques and facilities are available for defining the unusual or complicated situation.

For practical reasons, many diagnostic laboratories offer more extensive serologic diagnosis than cultural facilities for virus isolation. They will evaluate sera for the presence of antibodies to mumps virus. The serum for evaluation should be obtained as early as possible in the process, and a convalescent specimen should be obtained after an interval of 2 to 3 weeks. A pair of sera can determine whether a specific illness is mumps infection by demonstrating an increase in antibody titer. A single serum can determine whether a person has ever had mumps infection but cannot define when it occurred. As indicated above, there are several types of antibody elicited by mumps infection.

Treatment

There is no specific therapy available for mumps infection. Symptomatic management of patients includes adequate hydration and analgesic and antipyretic therapy.

Prophylaxis and Immunization

The problem repeatedly occurs of what to do after exposure to mumps infection. Usually the person concerned is an adult without previous symptomatic mumps infection. Hyperimmune globulin or pooled serum IgG has been administered after exposure, with no proven efficacy. However, there has been a controlled study purporting to demonstrate that the administration of hyperimmune globulin after the appearance of parotitis can decrease the incidence and severity of orchitis. For this reason, hyperimmune globulin has been administered to postpubertal males who already have parotitis.

There has been limited experience in Scandinavia using a formalin-inactivated mumps vaccine, which affords some short-term protection from infection. No anti-F protein antibodies are demonstrable. It is probable that the F protein, which is sensitive to formalin, is not present. However, animal studies suggest that whole virus preparations can only induce anti-HN antibodies when the virus fails to replicate in the host. Purified F protein is an effective immunogen, and antibody to this protein is necessary to limit cell-to-cell spread of virus.

Live attenuated mumps virus vaccine was licensed in January 1968 and is available for prophylactic use. It is recommended for administration to children more than 1 year old and to young adults for induction of immunity parallel to that induced by natural infection. Vaccine should not be given to pregnant women because of the potential vulnerability of the fetus. Although no data exist that demonstrate transmission of attenuated virus to the fetus, placental infection has been documented after maternal immunization. For practical purposes there is only a single serologic strain of mumps virus, hence a single infection with either natural or attenuated virus confers immunity. The vaccine is a live attenuated virus produced in tissue cultures of chick embryo fibroblasts and is administered parenterally. Virus is not shed by the vaccinee, and immunization does not cause any side effects. The vaccine produces 95 to 100 percent serologic conversion from antibody-negative to antibody-positive in vaccinated susceptibles. The antibody levels, although considerably lower, parallel those produced by natural infection and persist for the 12 to 15 years that vaccine has been available for

HAPTER 75

ubella (German Measles)

he mid-19th century until 1941, rubella was regard- benign childhood exanthem. When the Australian mologist, Sir Norman Gregg, reported the associa- intrauterine rubella infection with congenital cata- his attitude changed completely. Subsequently, s, congenital heart disease, and other malforma- ere found to result from maternal rubella during 4 months of pregnancy. The recovery in 1962 of irus in cell culture systems led to the development 1969, the licensure of attenuated active vaccines e proven safe and effective. Congenital rubella has infrequent in the United States as a result of wide- se of these vaccines.

he basis of its biochemical and biophysical prop- bella is classified as a togavirus, but it has no in- t with arthropod vectors. Because many different ay cause a similar clinical illness with rash and fe- only rubella is teratogenic, virus isolation tech- nd specific serologic tests for antibody have the necessary differentiation of etiologic agents.

Features and Pathogenesis

a mild rash disease that occurs principally in ut is seen at all ages. As shown in Figure 75-1, tion period is approximately 2 weeks, with mini- omal signs or symptoms. Most often, the first of illness is mild fever and respiratory signs im- preceding the onset of rash. The exanthem is es and papules, at first on the face and then on trunk, and extremities, where they remain d rarely coalesce. The rash has ordinarily disap- the third day. Preceding and accompanying the is lymphadenopathy, which may involve the r, suboccipital, and cervical nodes. Rash is ob- served commonly among children, but infection may be occult or only a febrile pharyngitis in as many as one third of adult patients. Although major complications are rare (thrombocytopenic purpura and encephalitis), the incidence of arthralgia and arthritis is much greater than generally appreciated. The frequency of joint involvement is directly correlated with increasing age and appears also to be more common among women. In a few patients, persistence of rubella virus in synovial cells has been associated with polyarthritis and arthralgia of lengthy duration. Usually joint involvement is acute and transient without sequelae (Fig. 75-1).

The route of infection is via the respiratory tract, with spread to lymphatic tissues and then to the blood. Both viremia and respiratory tract shedding of virus may precede the rash by 1 week, and the latter may follow it for another several weeks. Because much virus excretion occurs prior to the recognition of illness, secondary infection of intimate contacts has usually transpired before the primary patient has been diagnosed. Little is known of the actual pathology of the postnatal disease because it is not a fatal one. However, the pathogenesis of congenital infection has been well studied during and since the 1964 pandemic. Maternal viremia is followed by infection of the placenta, which may lead to virus invasion of the fetus. Multiple tissues and organs support the replication of virus, which continues to multiply throughout the remainder of pregnancy and in the postnatal period. A large percentage of maternal infections that occur in the first 3 months of pregnancy result in fetal illness. There is a diminishing number in the fourth month, and it is uncertain whether any fetal infections have resulted from maternal rubella in later pregnancy. Although the exact mechanism of damage to fetal organs is not clear, rubella infection of human embryonic cells in vitro is associated with both chromosomal breakage and inhibition of normal mitosis. Infants with